REMARKS

Applicants have amended claim 1. In particular, Applicants have amended claim 1 to add hydrogen to the Markush group of E. Support for this amendment may be found at least at page 8, line 20, and page 11, lines 15-16, of the specification. Also, Applicants have amended claim 1 to correct a typographical error. Further, Applicants have amended claim 11 to correct errors noted by the Examiner in paragraph 1 of the Office Action.

In response to the Restriction Requirement of Office Action dated February 3, 2003 in the above-referenced application, Applicants elect with traverse Group 1 (claims 1-10). In electing a particular species, Ar is phenanthridines, and E is somatostatin receptor binding molecules. As to positions for attachment of various groups, Applicants assert that they do not claim particular attachment of the various groups. Rather, Applicants claim a compound, and that compound may be targeted to a particular tissue.

However, Applicants respectfully assert that such a restriction is improper. At the outset, applicants note that all the claims are directed to the structure designated by the formula in claim 1. More specifically, claims 1-10 recite a compound, and claims 11-27 recite a method of performing a procedure by administering the compound designated by the formula of claim 1. Applicants now provide the following analysis in support of their assertion.

First, the Examiner's restriction forces applicants to fragment the invention they claimed within a single claim. Under *In re Weber, Soder, & Boksay*, 198 U.S.P.Q. 328, 331-32 (C.C.P.A. 1978) (copy attached) this is not permitted.

The invention in *Weber* related to cyclic diamine derivatives possessing a common psychotherapeutic property and was identified by a single generic formula expressed in Markush format. The instant invention relates to organic azides possessing a common physiological property and the derivatives are identified by a single generic formula (as in claim 1) expressed in Markush format.

In *Weber,* the court viewed the Examiner's restriction as tantamount to a refusal to examine. It held that the United States Patent and Trademark Office authority to restrict between claims of an application reciting one or more independent and distinct inventions, but does not have the authority to require an applicant to divide up a single claim and present it in different applications; this would allow an Examiner, rather than an applicant, to define an invention in violation of 35 U.S.C. §121, ¶2 ("The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention", emphasis added). Weber at 332. While recognizing the need for efficiency in limiting each application to one invention, the court stated that

> ...in drawing priorities between the Commissioner as administrator and the applicant as beneficiary of his statutory rights, we conclude that the statutory rights [of the applicant] are paramount.

Second, §803.02 of the MPEP states that if the claims have unity of invention, it is improper to refuse to examine "that which applicants regard as their

invention". Unity of invention exists where compounds included within a Markush group share a common utility and share a substantial structural feature as being essential to that utility.

With regard to the instant application, all the claimed compounds share an organic azide structure as shown in the formula of claim 1, and have the same utility as receptor-targeted azide derivatives and their bioconjugates for phototherapy of tumors and other lesions.

The Examiner, in the Restriction Requirement, has asked Applicants to cite the attachment of various groups, such as "L" to "E". However, Applicants assert that this is not the claimed invention. Applicants first note that they claim a <u>compound</u> having the recited structure which may bind to a cell via an epitope (E). Applicants do not claim the structure of the binding site between the compound and the target. Applicants also do not claim E for other than the recited targets. Thus, E includes compounds that direct the recited structure to the recited target site; Applicants' disclosure provides representative examples.

Applicants further respectfully assert that one skilled in the art would know structures of E based upon Applicants' description. For example, when using the composition for phototherapy of a prostate tumor, the chemical structure may contain a steroid hormone because prostate tumors are known to contain receptors for steroid hormones. One skilled in the art knows that steroid hormones are compounds containing the cyclopentanoperhydrophenanthrene ring, including but not limited to, the following: sterols such as cholesterol, bile acids such as cholanic acid, sex hormones

such as estrogens and androgens, adrenocortical hormones such as corticosteroids, cardiac glycosides such as digitoxigenin, sapogenins such as tigogenin, and alkaloids such as solasodine. Tietz (Ed.), Fundamentals of Clinical Chemistry, Third Edition, 1987, p. 554, W.B. Saunders Co., Philadelphia. Thus, the structure containing any of the above steroid hormones would bind to a cell that has a receptor for a steroid hormone. Selection of the particular steroid hormone is within the level of one skilled in the art; for example, an androgen for a prostate tumor.

Applicant respectfully asserts that one skilled in the art would know the identity of such compounds and would not require an exhaustive list of each and every compound that fits into each of applicants' claimed scope of E. For example, one skilled in the art knows that corticosteroids alone include its synthethic precursors of pregnenolone, progesterone, 17-hydroxypregnenolone, 17-hydroxprogesterone, 11-desoxycorticosterone, cortisol, corticosterone, aldosterone, cortisone, estrone, estraciol, androstenedione, testosterone, etiocholanolone, dehydroepandrosterone, as only a partial list.

The Examiner has further advised that the claims will be subject to rejection under 35 U.S.C. § 112 with regard to the definitions of "Ar" and the definition of "E" as hydrogen.

In particular, the Examiner states that the definitions of "Ar" do not adequately specify the nature and number of other substituents and/or multiple rings which are implied by the plural designations. In response, Applicants respectfully assert that one skilled in the art, based upon the specification, would know that

"benzenes", for example, is used in the general sense, that is, to encompass the group of compounds commonly referred to as benzenes, and not one particular compound. One example is the recitation at page 8, lines 17 et seq. that "Ar is an aromatic or heteroaromatic radical derived from the group consisting of benzenes, ..." These refer to the family of compounds, not one specific compound.

Also, the Examiner further particularly states that where E is hydrogen, the method would not appear to be operable, since there would be no moiety on the photosensitizer which would bind to a site requiring phototherapy. In response, Applicants note that at page 15, lines 17-21, it is described that an additional attachment of a binding group may not be necessary where the aromatic azido compounds themselves preferentially accumulate in the target tissue. There, the application gives the example that if Ar is an anthracycline moiety, it will bind to cancer cells directly and not require an epitope for targeting purposes.

Conclusion

For the reasons discussed, Applicants respectfully request that the Examiner reconsider the restriction requirement.

Applicant believes that no fee is due. If, however, any additional fee or surcharges are deemed due, please charge same or credit any overpayment to deposit account no. 23-3000.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "Version with Markings to Show Changes Made."

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 1 and 11 have been amended as follows:

1. (Amended) An organic azide compound having the formula:

$$E—L—Ar—X—N_3$$

wherein Ar is an aromatic or a heteroaromatic radical derived from the group consisting of benzenes, polyfluorobenzenes, naphthalenes, naphthoquinones, anthracenes, anthraquinones, phenanthrenes, tetracenes, naphthacenediones, pyridines, quinolines, isoquinolines, indoles, isoindoles, pyrroles, imidiazoles, pyrazoles, pyrazines, purines, benzimidazoles, benzofurans, dibenzofurans, carbazoles, acridines, acridones, phenanthridines, thiophenes, benzothiophenes, dibenzothiophenes, xanthenes, xanthones, flavones, coumarins, and anthacylines;

E is selected from the group consisting of <u>hydrogen,</u> somatostatin receptor binding molecules, ST receptor binding molecules, neurotensin receptor binding molecules, bombesin receptor binding molecules, CCK receptor binding molecules, steroid receptor binding molecules, and carbohydrate receptor binding molecules;

L is selected from the group consisting of $-(CH_2)_a-$, $-(CH_2)_bCONR^1-$, $-N(R^2)CO(CH_2)_c-$, $-OCO(CH_2)_d-$, $-(CH_2)_eCO_2-$, -OCONH-, $-OCO_2-$, -HNCONH-, -HNCSNH-, -HNNHCO-, $-OSO_2-$, $-NR^3(CH_2)_eCONR^4-$, $-CONR^5(CH_2)_fNR^6CO-$, and $-NR^7CO(CH_2)_gCONR^8-$;

X is either a single bond or is selected from the group consisting of $-(CH_2)_h-$, -OCO-, -HNCO-, $-(CH_2)_iCO-$, and $-(CH_2)_jOCO-$;

R^1 to R^8 are independently selected from the group consisting of hydrogen, C1-C10 alkyl, -OH, C1-C10 polyhydroxyalkyl, C1-C10 alkoxyl, C1-C10 alkoxyalkyl, $-SO_3H$, $-(CH_2)_kCO_2H$, and $-(CH_2)_lNR^9R^{10}$;

R^9 and R^{10} are independently selected from the group consisting of hydrogen, C1-C10 alkyl, C5-C10 aryl, and C1-C10 polyhydroxyalkyl; and

[subscripts] a to l independently range from 0 to 10.

11. (Twice Amended). A method of performing a phototherapeutic procedure which comprises:

(a) administering to a target tissue in an animal an effective amount of an organic azide photosensitizer having the formula

$$E—L—Ar—X—N_3$$

wherein Ar is an aromatic or a heteroaromatic radical derived from the group consisting of benzenes, polyfluorobenzenes, naphthalenes, naphthoquinones, anthracenes, anthraquinones, phenanthrenes, tetracenes, naphthacenediones, pyridines, quinolines, isoquinolines, indoles, isoindoles, pyrroles, imidiazoles, pyrazoles, pyrazines, purines, benzimidazoles, benzofurans, dibenzofurans, carbazoles, acridines, acridones, phenanthridines, thiophenes, benzothiophenes, dibenzothiophenes, xanthenes, xanthones, flavones, coumarins, and anthacylines; E is a hydrogen atom or is selected from the group consisting of somatostatin receptor binding molecules, ST receptor binding molecules, neurotensin receptor binding molecules, bombesin receptor binding molecules, CCK receptor binding molecules, steroid receptor binding molecules, and carbohydrate receptor binding molecules; L is selected from the group consisting of $-(CH_2)_a-$, $-(CH_2)_bCONR^1-$, $-N(R^2)CO(CH_2)_c-$, $-OCO(CH_2)_d-$, $-(CH_2)_eCO_2-$, -OCONH-, $-OCO_2-$, -HNCONH-, -HNCSNH-, -HNNHCO-, $-OSO_2-$, $-NR^3(CH_2)_eCONR^4-$, $-CONR^5(CH_2)_fNR^6CO-$, and $-NR^7CO(CH_2)_gCONR^8-$; X is either a single bond or is selected from the group consisting of $-(CH_2)_h-$, -OCO-, -HNCO-, $-(CH_2)_iCO-$, and $-(CH_2)_jOCO-$; R^1 to R^8 are independently selected from the group consisting of hydrogen, C1-C10 alkyl, -OH, C1-C10 polyhydroxyalkyl, C1-C10 alkoxyl, C1-C10 alkoxyalkyl, $-SO_3H$, $-(CH_2)_kCO_2H$, and $-(CH_2)_lNR^9R^{10}$; R^9 and R^{10} are independently selected from the group consisting of hydrogen, C1-C10 alkyl, C5-C10 aryl, and C1-C10 polyhydroxyalkyl; and subscripts a to l independently range from 0 to 10; and

(b) exposing said target tissues with the light of wavelength between 300 and 950 nm with sufficient power and fluence rate to perform the phototherapeutic procedure.